UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/612,925	07/10/2000	Carlos Antonio Durate Cano	P-13 Div II	9520

7590 03/26/2003

Lackenbach Siegel Marzullo Aronson & Greenspan PC
One Chase Road
Scarsdale, NY 10583

EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	18

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/612,925	Cano et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 12, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *11* is/~~are~~ pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *11* is/~~are~~ rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. *08/930,917* .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☒ Interview Summary (PTO-413) Paper No(s). 15 & 16 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' amendments filed 007/10/00 and 03/12/03 (paper no. 1 and 17).

Status of Claims

2) Claims 1-10 and 12-19 have been canceled via the amendment filed 07/10/00.

Claim 11 is pending and is under examination.

Sequence Listing

3) The CRF from the parent application, SN 08/930,917, has been transferred to the instant case as per Applicants' request filed 03/12/03 (paper no. 17).

Drawings

4) The drawings submitted in the instant case are not objected to by the Draftsperson under 37 C.F.R 1.84 or 1.152 and as such, the drawings have been approved as formal drawings.

Priority

5) Acknowledgment is made of Applicants' submission in the parent application, SN 08/930,917, of the certified copy of the priority document, 10/96, filed 01/17/96 in Cuba.

The instant application is a Divisional application of SN 08/930,917, which was filed as a national stage 371 application of the PCT application, PCT/CU97/00001, filed 01/17/1997, with a priority claim to application, 10/96, filed 01/17/1996 in Cuba.

Abstract

6) The abstract of the instant specification is objected to because the number of words contained in the abstract exceeds the number of words permitted. See M.P.E.P § 608.01(b). Correction is required.

Specification - Informalities

7) The instant specification is objected to for the following reasons:

(a) The first paragraph of the instant specification does not disclose the priority/continuity status. The first paragraph of the specification needs to be amended, as indicated above under 'Priority', to include details of the prior application(s) to which priority is

claimed.

(b) The specification is objected to for not leaving sufficient margin at the top of each page such that holes can be punctured in order to secure the application pages in the case binder. A substitute specification is required, because the holes at the top of some pages of the instant specification have made lines/words unreadable. Each page must include a top margin of at least 2.0 cm. See M.P.E.P 600. The substitute specification filed must be accompanied by a statement that it contains no new matter. Such a statement must be a verified statement if made by a person not registered to practice before the Office.

(c) A part of the instant specification on pages 11 and 12 contains single-spaced text making future amendment entries into these parts of the specification difficult. Amendment to the specification is required presenting lines that are properly spaced allowing easy entry of amendments.

(d) The Figure descriptions for Figures 9 and 10 are incorrect. Individual Figure descriptions in the specification on page 17 should be amended to read Figures 9A and 9B and Figures 10A, 10B and 10C. All references to these Figures in the specification should be amended to reflect these changes in numbering.

(e) The use of the trademark in the instant specification has been noted. For example, see page 15, second full paragraph: "Triton-X-100". The recitation should be capitalized wherever it appears and be accompanied by the generic terminology. Each letter of the trademark must be capitalized. See M.P.E.P 608.01(V) and Appendix I. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to trademark recitations, wherever such recitations appear.

(f) Certain terminologies in the instant specification are not understood. For example, "adyuvated" on page 7, line 25; "adyuved" on page 13, line 33; "alicuoted" on page 7, line 29; "hybrofobicity" on page 7, line 20; "tricloroacetic acid" on page 7, line 22; "subunity" on page 4, line 34; and "citosol" on page 2, lines 2 and 9. It is suggested that Applicants review the entire specification as these are only a few examples of such errors and make necessary amendments.

Applicants are cautioned about the entry of new matter when amending the specification.

(g) Many of the prior art references cited throughout the specification lack date of publication. For example, see page 2, Kiefhaber *et al*, Denton *et al.*, Del Val *et al.* and Etlinger *et al.* Correction is requested.

(h) Claim 11 is objected to for being in a single-spaced format making future amendment entries difficult. Correction is requested.

(i) The amino acid or nucleotide sequences recited in Figures 1, 3, 5, 6 and 8 contain more than four amino acids or 10 nucleotide bases, yet are not identified either on the drawings or under the 'Description of the Figures' on page 16 and 17 of the specification by a SEQ ID NO. as required under 37 C.F.R 1.821 through 1.825. Any sequences recited in the instant specification which are encompassed by the definitions for nucleotide and/or amino acid sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2) must comply with the requirements of 37 C.F.R 1.821 through 1.825. Note that branched sequences are specifically excluded from this definition.

APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R 1.821(g).

Rejection(s) under 35 U.S.C. § 101

8) Claim 11 is rejected under 35 U.S.C. § 101 as being directed to a non-statutory subject matter. The claim reads on products of nature. The claim lacks limitations which distinguish this product from those that may exist naturally. Consequently, the claim does not embody patentable subject matter as defined in 35 U.S.C § 101. See MPEP 2105. The rejection can be obviated by amending the claim to recite --An isolated .... antibody.....-- in connection with the product to reflect the hands of the inventors in the production or creation of the recited product as such a recitation has descriptive support in the paragraph bridging pages 13 and 14 of the specification.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

9) Claim 11 is rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological material is (1)

known and readily available to the public; (2) reproducible from the written description, e.g. sequenced; or (3) deposited.

Claim 11 is directed to a monoclonal antibody, recited as "448/30/7". It is apparent that the hybridoma secreting this monoclonal antibody is required to practice the claimed invention. As a required element, the hybridoma producing the monoclonal antibody must be known and be readily available to the public, or obtainable by a reproducible method set forth in the specification, or otherwise be readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the hybridoma producing the monoclonal antibody. From the instant specification, it does not appear that the hybridoma producing the monoclonal antibody designated as "448/30/7" is deposited at a recognized depository. The monoclonal antibody does not appear to be readily available to the public and it is unclear if the cell line producing the antibody can be reproducibly isolated without undue experimentation. Since obtaining such a monoclonal antibody with specificity for the recited stabilizer is uncertain and non-predictable, undue experimentation would have been required to practice the invention. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: 1) a cell line; 2) the cell line which produces the chemically and functionally distinct antibody; and/or 3) the claimed antibody amino acid sequence is an unpredictable event. Deposit of the hybridoma producing 448/30/7 monoclonal antibody would satisfy the requirements of 35 U.S.C. § 112, first paragraph.

If a deposit has already been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by Applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each state.

The specification should be amended to include complete deposit information for the hybridoma producing the recited antibody including the full address of the depository and the date of deposition. Additionally, Applicants are requested to amend the specification and the claim(s) with the proper information regarding the depository number and provide evidence to support the insertion for the depository number. As a means of satisfying the necessary criteria of the deposit rules and to show that the deposited hybridoma cell line producing the claimed antibody is the same as the one deposited, Applicants may submit a copy of the contract or a notice of acceptance of the cell line(s) by the depository.

Applicants' attention is directed to *In re Lundack*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 C.F.R § 1.801-1.809 for further information concerning deposit practice.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

10) Claim 11 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 11 is vague in the recitation "448/30/7". The recitation of what appears to be a laboratory designation does not clearly define the claimed monoclonal antibody. Amending the claim to identify the monoclonal-producing cell line by its deposit number is suggested for clarity.

(b) Claim 11 is vague, indefinite and confusing in reciting a monoclonal antibody and following it with the limitation "and it is used for the immunodetection and purification of any protein fused to said stabilizer peptide". The claim is poorly written and is not proper form.

(c) Claim 11 is further vague in the recitation "P64K antigen" without particularly pointing out the nature of the antigen? Is this a protein or polypeptide antigen, glycoprotein antigen or peptide antigen?

(d) Claim 11 is indefinite in the recitation "peptide derived from the first 47 amino acids of the N-terminal end". It is not clear what is encompassed in the limitation 'derived'? Does it mean that the stabilizer peptide consists of the first 47 amino acid residues of the N-terminal end of the P64K antigen, or any smaller peptides of any size within the first 47 amino acid residues?

Rejection(s) under 35 U.S.C. § 102

11) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12) Claim 11 is rejected under 35 U.S.C. § 102(b) as being anticipated by Nazabal *et al.* (*In*: *Neisseria* 94. Proceedings of the Ninth International Pathogenic *Neisseria* Conference. (Ed) Evans *et al.* 26-30 September, Winchester, England, pages 98-99, 1994).

Nazabal *et al.* taught monoclonal antibodies specific to three different epitopes of the 64k protein of *Neisseria meningitidis*, B:4:P1.15 (see third full paragraph).

The Applicants' monoclonal antibody is viewed as the same as the prior art monoclonal antibody. Although Nazabal *et al.* do not identify their monoclonal antibody as having the designation, "448/30/7", the mere identification of the same monoclonal antibody already taught in the prior art with a different laboratory designation, imparts neither novelty nor unobviousness to the antibody. Therefore, Applicants' "448/30/7" monoclonal antibody is viewed as the same as one of the prior art monoclonal antibodies, but given a different laboratory designation, absent evidence to the contrary. Since the Office does not have the facilities for examining and comparing Applicants' 448/30/7 monoclonal antibody with that of the prior art monoclonal antibody, the burden is on the Applicants to show a novel or an unobvious difference between the instantly claimed monoclonal antibody and the prior art monoclonal antibody, i.e., to show that the prior art monoclonal antibody does not possess the same material and functional characteristics of the instantly recited monoclonal antibody. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzerald et al.*, 05 USPQ 594.

Claim 11 is anticipated by Nazabal *et al.*

Rejection(s) under 35 U.S.C. § 103

13) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

14) Claim 11 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Rodriguez *et al.* (EP 0,474,313 A2) or Niebla *et al.* (*In: Neisseria 94, Proceedings of the Ninth International Pathogenic Neisseria Conference*, (ed) Evans *et al.*, Winchester, England, 26-30 September 1994, pages 85-86).

The monoclonal antibody, 448/30/7, recited in the instant claim is viewed as 'a' monoclonal antibody specific to a peptide from the first 47 amino acids to the N terminal end of the P64k antigen of *Neisseria meningitidis* B:4:P1.15, since the claim does not identify a specific hybridoma cell line from which the monoclonal antibody is secreted, and does not provide the deposit or accession number.

Rodriguez *et al.* taught the N-terminal portion of the P64k antigen of *Neisseria meningitidis* B:4:P1.15 and identify the amino acid sequence, SEQ ID NO: 3 (see page 7, fifth full paragraph; lines 1-17 on page 19; and first full paragraph in Example 3). Rodriguez *et al.* taught hybridoma cells secreting monoclonal antibodies specific against the P64k antigen for studying their bactericidal activity against different strains of *Neisseria meningitidis* in a bactericidal test (see Example 6 and claim 11).

Niebla *et al.* taught a fusion protein comprising the first 46 amino acids of the N-terminus of the P64k antigen of *Neisseria meningitidis* B:4:P1.15 fused to a heterologous protein such as the *porA* protein of *Neisseria meningitidis*. The immunogenicity and the bactericidal activity of the protein was evaluated by immunization of mice with the protein along with a suitable adjuvant (see page 85).

Rodriguez *et al.* or Niebla *et al.* do not expressly teach a monoclonal antibody specific to the N-terminal portion of the P64k antigen of *Neisseria meningitidis* B:4:P1.15. However, methods of preparing specific monoclonal antibodies via hybridoma technology was well known and routinely practiced in the art at the time of the invention, for instance, as taught by Rodriguez *et al.*

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a monoclonal antibody to Rodriguez's N-terminal portion of the P64k antigen of *Neisseria meningitidis* B:4:P1.15 or Niebla's 46 amino acid-long N-terminus of the P64k antigen of *Neisseria meningitidis* B:4:P1.15 using art-known hybridoma technology to produce the instant invention, with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a monoclonal antibody reagent reactive with the P64K protein of *Neisseria meningitidis*, or with the N-terminal of the P64k protein antigen of *Neisseria meningitidis* so that its bactericidal ability against different strains of *Neisseria meningitidis* could be studied as taught by Rodriguez *et al.*

Claim 11 is *prima facie* obvious over the prior art of record.

Remarks

15) Claim 11 stands rejected.

16) Papers related to this application may be submitted to Group 1600, AU 1641 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1 (CM1). The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242 which receives papers 24 hours a day, 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

March, 2003

S. DEVI, PH.D.
PRIMARY EXAMINER